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### Figure 1

F F L L L GAC ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA +1 10 S Q **V** Q L E A G TGG GTC TTG TCC CAG GTG CAG CTG CAG GAG GCG GGC CCA GGA CTG GTG 20 L AAG CCT TCG GAG ACC CTG TCC CTC ACC TGC AGT GTC TCT GGT GGC TCC 30 40 S G F Ι R Q P ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA GGG AAG 50 60 I G Y I Y S G G G GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT 70 N N S I TAC AAT CCC TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC 80 90 F S L K L R S V AAG AAC CTC TTC TCC CTG AAA CTG AGG TCT GTG ACC GCC GCG GAC ACG 100 I L A S N K Y GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT CAC TGG TTA 110 120 Y Q V L ·V T W G G S S TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC



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### Figure 2

L L L +1 S È L Y S V P R GAC TCT GCG GCC TCC TAT GAG TTG AGT CAG CCT CGC TCA GTG TCC GTG 20 T C G G TCC CCA GGA CAG ACG GCC GGG TTC ACC TGT GGG GGA GAC AAC GTT GGA 30 40 R Y Q Q K P P Q AGG AAA AGT GTA CAG TGG TAC CAG CAG AAG CCA CCG CAG GCC CCT GTG 50 60 I A D S E R ₽ S G I CTG GTC ATC TAT GCT GAC AGC GAA CGG CCC TCA GGG ATC CCT GCG CGA 70 S G N T A T L TTC TCT GGC TCC AAC. TCA GGG AAC ACC GCC ACC CTG ACC ATC AGC GGG 80 90 A D Y Y D GTC GAG GCC GGG GAT GAG GCT GAC TAT TAC TGT CAG GTG TGG GAC AGT 100 F G G G ACT GCT GAT CAT TGG GTC TTC GGC GGA GGG ACC CGG CTG ACC GTC CTA

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Thr Glu Cys Ser TER ACA GAA TGT TCA TGA Appin. No.: 09/612,914
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### 3/32 Figure 3

Frame	<b>=</b> 1	Met ATG	Ala GCC	Trp TGG 9	Ala GCT	Leu CTG	Leu CTG 18	Leu	Leu	Gly GGC 27	Leu CTC	Leu CTT	Ala GCT 36	His CAC	Phe TTT	Thr ACA 45	Asp GAC	Ser TCT	Ala GCG 54	Ala GCC
Ser TCC	Tyr TAT	Glu GAG 66	Leu TIG	Ser AGT	Gln CAG 75	Pro CCT	Arg CGC	Ser TCA 84	Val GTG	Ser TCC	Val GTG 93	Ser TCC	Pro CCA	Gly GGA 102	Gln CAG	Thr ACG	Ala GCC 111	Gly GGG	Phe TTC	Thr ACC 120
Cys TGT	Gly GGG	Gly GGA 129	Asp GAC	Asn AAC	Val GTT 138	Gly GGA	Arg AGG	Lys AAA 147	Ser AGT	Val GTA	Gln CAG 156	Trp TGG	Tyr TAC	Gln CAG 165	Gln CAG	Lys AAG	Pro CCA 174	Pro CCG	Gln CAG	Ala GCC 183
Pro CCT	Val GTG	Leu CTG 192	Val GTC	Ile ATC	Tyr TAT 201	Ala GCT	Asp GAC	Ser AGC 210	Glu GAA	Arg CGG	Pro CCC 219	Ser TCA	Gly GGG	Ile ATC 228	Pro CCT	Ala GCG	Arg CGA 237	Phe TTC	Ser TCT	Gly GGC 246
Ser TCC	Asn AAC	Ser TCA 255	Gly GGG	Asn AAC	Thr ACC 264	Ala GCC	Thr ACC	Leu CTG 273	Thr ACC	Ile ATC	Ser AGC 282	Gly GGG	Val GTC	Glu GAG 291	Ala GCC	Gly GGG	Asp GAT 300	Glu GAG	Ala GCT	Asp GAC 309
Tyr TAT	Tyr TAC	Cys TGT 318	Gln CAG	Val GTG	Trp TGG 327	Asp GAC	Ser AGT	Thr ACT 336	Ala GCT	Asp GAT	His CAT 345	Trp TGG	Val GTC	Phe TIC 354	Gly GGC	GGY GJÀ	Gly GGG 363	Thr ACC	CGG Yrg	Leu CTG 372
Thr ACC	Val GTC	Leu CTA 381	Gly GGT	Gln CAG	Pro CCC 390	Lys AAG	Ala GCT	Ala GCC 399	Pro CCC	Ser TCG	Val GTC 408	Thr ACT	Leu CTG	Phe TTC 417	Pro CCG	Pro CCC	Ser TCC 426	Ser TCT	Glu GAG	Glu GAG 435
Leu CTT	Gln CAA	Ala GCC 444	Asn AAC	Lys AAG	Ala GCC 453	Thr ACA	Leu CTG	Val GTG 462	Cys TGT	Leu CTC	Ile ATA 471	Ser AGT	Asp GAC	Phe TTC 480	Tyr TAC	Pro CCG	Gly GGA 489	Ala GCC	Val GTG	Thr ACA 498
Val GTG	Ala GCC	Trp TGG 507	Lys AAG	GCA	Asp GAT 516	Ser AGC	AGC	Pro CCC 525	Val GTC	Lys AAG	Ala GCG 534	Gly GGA	Val GTG	Glu GAG 543	Thr ACC	Thr ACC	Thr ACA 552	Pro CCC	Ser TCC	Lys AAA 561
G <u>l</u> n CAA	Ser AGC	Asn AAC 570	Asn AAC	Lys AAG	Tyr TAC 579	Ala GCG	Ala GCC	Ser AGC 588	Ser AGC	Tyr TAC	Leu CTG 597	Ser AGC	Leu CTG	Thr ACG 606	Pro CCT	Glu GAG	Gln CAG 615	Trp TGG	Lys Lys	Ser TCC 624
His CAC	Arg AGA	Ser AGC 633	Tyr TAC	Ser AGC	Cys TGC 642	Gln CAG	Val GTC	Thr ACG 651	His CAT	Glu GAA	Gly GGG 660	Ser AGC	Thr ACC	Val GTG 669	Glu GAG	Lys AAG	Thr ACA 678	Val GTG	Ala GCC	Pro CCT 687



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# <sup>4/32</sup> Figure 4a

Frame 1	Met ATG	Lys AAA	His CAC 9	Leu CTG	ITP TEG	Phe TTC 18	Phe TTC	CTC	Leu CTC 27	Leu CTG	Val GIG	Ala GCA 36	Ala GCC	Pro	Arg AGA 45	Trp TGG	Val GTC	Leu TTG 54	Ser TCC
Gln Val CAG GTG	Gln CAG 66	Leu CTG	Gln CAG	Glu GAG 75	Ser TCG	Gly GGC	Pro CCA 84	Gly GGA	Leu CTG	Val GTG 93	Lys AAG	Pro CCT	Ser TCG 102	Glu GAG	Thr ACC	Leu CTG 111	Ser TCC	Leu CTC	Thr ACC 120
Cys Ser TGC AGT	Val GTC 129	Ser TCT	Gly GGT	Gly GGC 138	Ser TCC	Ile ATC	Ser AGC 147	Gly GGT	GAC Asp	Tyr TAT 156	Tyr TAT	Trp TGG	Phe TTC 165	Trp TGG	Ile ATC	Arg CGC 174	Gln CAG	TCC	Pro CCA 183
Gly Lys GGG AAG	Gly GGA 192	Leu CTG	Glu GAG	Trp TGG 201	Ile ATC	Gly	Tyr TAC 210	Ile ATC	Tyr Tat	Gly GGC 219	Ser AGT	Gly GGT	Gly GGG 228	Gly GGC	Thr ACC	Asn AAT 237	Tyr TAC	TAA	Pro CCC 246
Ser Leu TCC CTC	Asn AAC 255	Asn AAT	Arg CGA	Val GTC 264	Ser TCC	ATT	Ser TCA 273	Ile ATA	Asp GAC	Thr ACG 282	Ser TCC	Lys AAG	Asn AAC 291	Leu CTC	Phe TTC	Ser TCC 300	Leu CTG	AAA	Leu CTG 309
Arg Se: AGG TC:	val GTG 318	ACC	Ala GCC	Ala GCG 327	Asp GAC	Thr ACG	Ala GCC 336	Val GTC	Tyr TAT	Tyr TAC 345	Cys TGT	Ala GCG	Ser AGT 354	Asn AAT	Ile ATA	Leu TTG 363	Lys AAA	Tyr TAT	Leu CTT 372
His Tr CAC TG	p Leu 3 TTA 381	TTA	TYT TAC	Trp TGG 390	GGC	Gln CAG	Gly GGA 399	GIC	Leu CTC	Val GTC 408	ACC	Val	Ser TCC 417	TCA	Ala GCT	Ser AGC 426	ACC	Lys AAG	Gly GGC 435
Pro Se CCA TC	r Val C GTC 444	TTC	Pro	Leu CTG 453	GCG	Pro	Cys TGC 462	TCC	Arg	Ser AGC 471	ACC	Ser TCC	Glu GAG 480	AGC	Thr	Ala GCC 489	GCC	Leu CTG	Gly GGC 498
Cys Le	val GGTC 507	AAG	Asp GAC	TYT TAC 516	TTC	Pro	Glu GAA 525	CCG	Val	Thr ACG 534	GTG	Ser TCG	Trp TGG 543	AAC	Ser TCA	Gly GGC 552	GCC	Leu CTG	Thr ACC 561
Ser Gl	y Val C GTC 570	CAC	Thr.	Phe TTC 579	CCG	Ala GCT	Val GTC 588	CTA	Gln CAG	Ser FCC 597	TCA	Gly GCA	Leu CTC	TAC	Ser	Leu CTC 615	AGC	Ser AGC	Val GTG 624
Val Th GTG AC	r Val C GTC 633	CCC	Ser TCC	Ser AGC 642	AGC	Leu	Gly GGC 651	ACG	Lys AAG	Thr ACC 660	TAC	Thr ACC	Cys TGC 669	AAC	Val	Asp GAT 678	CYC	Lys AAG	Pro CCC 687
Ser As	n The	- Lys	Val	. Asp	Lys	Arg	Val	Glu	Ser	Lys	Тут	Gly	Pro	Pro	Cys	Pro	Ser	Cys	Pro



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### Figure 4b

AGC	AAC	ACC 696	AAG	GI	GAC 705	AAG	AGA	GTT 714	GAG	TCC	723	TAT	GGT	CCC 732	CCA	TGC	CCA 741	TCA	TGC	CCA 750
Ala GCA	Pro CCT	Glu GAG 759	110	Let	Gly GGG 768	GGW	Pro CCA	Ser TCA 777	Val GTC	Phe	Leu CIG 786	TTC	Pro	Pro CCA 795	Lys AAA	Pro	Lys AAG 804	Asp GAC	The	Leu CTC 813
Met ATG	Ile	Ser TCC 822	Arg CGG	Thr	Pro CCT 831	GAG	Val GTC	Thr ACG 840	Cys TGC	Val GTG	Val GIG 849	Val GTG	Asp GAC	Val GTG 858	Ser AGC	Gln CAG	Glu GAA 867	Asp GAC	Pro	GAG
Val GTC	Gln CAG	Phe TTC 885	Asn AAC	Trp	Tyr TAC 894	Val GTG	Asp GAT	Gly GGC 903	Val GTG	Glu GAG	Val GTG 912	His CAT	Asn AAT	Ala GCC 921	Lys AAG	Thr ACA	Lys AAG 930	Pro CCG	Arg CGG	Glu GAG 939
Glu GAG	Gln CAG	Phe TTC 948	Asn AAC	Ser AGC	The ACG 957	Tyr TAC	Arg CGT	Val GTG 966	Val GTC	Ser AGC	Val GIC 975	Leu CTC	Thr ACC	Val GTC 984	Leu CTG	His CAC	Gln CAG 993	Asp GAC	TGG	Leu CTG .002
Asn AAC		Lys AAG 1011	Glu GAG	TAC	Lys AAG 1020	Cys TGC	AAG	Val GTC .029	Ser TCC	AAC	Lys 8E01	Gly GGC	CTC	Pro CCG L047	Ser TCC	TCC	Ile ATC L056	Glu GAG	AAA	Thr ACC .065
Ile ATC	TCC	Lys AAA 1074	Ala GCC	AAA	Gly GGG 1083	Gln CAG	CCC	Arg CGA .092	Glu GAG	CCA	Gln CAG L101	Val GTG	TAC	Thr ACC	Leu CTG	CCC	Pro CCA L119	Ser TCC	CAG	Glu GAG 128
Glu GAG	AIG	Thr ACC 137	Lys AAG	AAC	Gln CAG 1146	Val GTC	AGC	Leu CTG 155	Thr ACC	TGC	Leu CTG 1164	Val GTC	AAA	Gly GGC 173	Phe TTC	TAC	Pro CCC L182	Ser AGC	GAC	Ile ATC 191
Ala GCC	GIG	Glu GAG 200	Trp TGG	حالتك	Ser AGC 1209	Asn AAT	فافافا	Gln CAG 218	Pro CCG	GAG	Asn AAC .227	Asn AAC	TAC	Lys AAG .236	Thr ACC	ACG	Pro CCT 1245	Pro CCC	GTG	Leu CTG 254
Asp GAC	rcc	Asp GAC 263	Gly GGC	TCC	Phe TTC 1272	Phe TTC	CIC	Tyr TAC 281	Ser AGC	AGG	Leu CTA .290	Thr ACC	GTG	Asp GAC 299	Lys AAG	AGC	Arg AGG .308	Trp TGG	CAG	Glu GAG 317
Gly GGG	WWT.	Val GTC 326	Phe TTC	TCA	Cys TGC 1335	Ser TCC	GIG .	Met ATG 344	His CAT	GAG	Ala GCT .353	Leu CTG	CAC	Asn AAC 362	His CAC	TAC	Thr ACA .371	Gln CAG	aac .	Ser AGC 380
Leu CTC	TCC	Leu CTG 389	Ser TCT	CTG	Gly GGT	Lys AAA	TER TGA		·											



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### Figure 5a



Frame 1	Met ATG	Lys AAA	His CAC 9	Leu	Trp TGG	Phe TTC 18	Phe	Leu	Leu CTC 27	CIG	Val GTG	Ala GCA 36	Ala GCC	Pro	Arg AGA 45	Trp TGG	Val GTC	Leu TTG 54	Ser TCC
Glm Val CAG GTG	Gln CAG 66	Leu CTG	Gln CAG	Glu GAG 75	Ser TCG	Gly GGC	Pro CCA 84	GGA	Leu CTG	Val GIG 93	Lys AAG	Pro CCT	Ser TCG 102	Glu GAG	Thr ACC	Leu CTG 111	Ser TCC	CIC	Thr ACC 120
Cys Ser TGC AGT	Val GTC 129	Ser TCT	Gly GGT	Gly GGC 138	Ser	Ile ATC	Ser AGC 147	Gly GGT	Asp GAC	Tyr TAT 156	Tyr TAT	Trp TGG	Phe TTC 165	Trp TGG	Ile ATC	Arg CGC 174	Gln CAG	Ser TCC	Pro CCA 183
Gly Lys GGG AAG	Gly GGA 192	Leu CTG	Glu GAG	Trp TGG 201	Ile ATC	Gly GGC	Tyr TAC 210	Ile ATC	Tyr TAT	Gly GGC 219	Ser AGT	Gly GGT	Gly GGG 228	Gly GGC	Thr ACC	Asn AAT 237	Tyr TAC	Asn TAA	Pro CCC 246
Ser Leu TCC CTC	Asn AAC 255	Asn AAT	Arg CGA	Val GTC 264	Ser TCC	Ile ATT	Ser TCA 273	Ile ATA	Asp GAC	Thr ACG 282	Ser TCC	Lys AAG	Asn AAC 291	Leu CTC	Phe TTC	Ser TCC 300	Leu CTG	Lys AAA	Leu CTG 309
Arg Ser AGG TCT	Val GTG 318	Thr ACC	Ala GCC	Ala GCG 327	Asp GAC	Thr ACG	Ala GCC 336	Val GTC	Ty: TXT	Tyr TAC 345	Cys TGT	Ala GCG	Ser AGT 354	Asn AAT	Ile ATA	Leu TTG 363	Lys AAA	Tyr TAT	Leu CTT 372
His Trp CAC TGG	Leu TTA 381	Leu TTA	Tyr TAC	Trp TGG 390	Gly GGC	Gln CAG	GCA 399	Val GIC	Leu CTG	Val GTC 408	Thr ACC	Val GTC	Ser TCC 417	Ser TCA	Ala GCT	Ser AGC 426	Thr ACC	Lys AAG	Gly GGG 435
Pro Ser CCA TCC	Val GTC 444	Phe TIC	Pro CCC	Leu CTG 453	Ala GCG	Pro CCC	Cys TGC 462	Ser TCC	Arg AGG	Ser AGC 471	Thr ACC	Ser TCC	Glu GAG 480	Ser AGC	Thr ACA	Ala GCC 489	Ala GCC	Leu CTG	Gly GGC 498
Cys Leu TGC CTG	Val GTC 507	Lys AAG	Asp GAC	Tyr TAC 516	Phe TTC	Pro CCC	Glu GAA 525	Pro CCG	Val GTG	Thr ACG 534	Val GTG	Ser TCG	Trp TGG 543	Asn AAC	Ser TCA	Gly GGC 552	Ala GCC	Leu CTG	Thr ACC 561
Ser Gly AGC GGC	Val GTG 570	His CAC	Thr ACC	Phe TTC 579	P±0 CCG	Ala GCT	Val GTC 588	Leu CTA	Gln CAG	Ser TCC 597	Ser TCA	GGA GGA	Leu CTC 606	Tyr TAC	Ser TCC	Leu CTC 615	Ser AGC	Ser AGC	Val GTG 624
Val Thr	Val GTG 633	Pro CCC	Ser TCC	Ser AGC 642	Ser AGC	Leu TTG	Gly GGC 651	Thr ACG	Lys AAG	Thr ACC 660	Tyr TAC	Thr ACC	Cys TGC 669	Asn AAC	Val GTA	Asp GAT 678	His CAC	A4C	Pro CCC 687
Ser Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Ser	Cys	Pro



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### Figure 5b

AGC AAC	ACC 2 696	AAG (	GTG	GAC 705	AAG	AGA	GIT 714	GAG	TCC	<b>AAA</b> 723	TAT	ggt	CCC 732	CCA	TGC	CCA 741	TCA	TGC	ССА 750
Ala Pro GCA CCT	Glu 1 GAG 7 759	Phe (	Glu GAG	Gly GGG 768	Gly GGA	Pro CCA	Ser TCA 777	Val GIC	Phe TTC	Leu CIG 786	Phe TTC	Pro CCC	Pro CCA 795	Lys AAA	Pro CCC	Lys AAG 804	GAC Asp	Thr ACT	Leu CTC 813
Met Ile ATG ATC	Ser A TCC 0 822	Arg : CGG 1	Thr ACC	Pro CCT 831	Glu GAG	Val GIC	Thr ACG 840	Cys TGC	Val GTG	Val GTG 849	Val GTG	Asp GAC	Val GTG 858	Ser AGC	Gln CAG	Glu GAA 867	Asp GAC	Pro	Glu GAG 876
Val Gln GTC CAG	Phe 1 TTC 1 885	Asn (	Trp IGG	Tyr TAC 894	Val GTG	Asp GAT	Gly GGC 903	Val GTG	Glu GAG	Val GTG 912	CAT	Asn AAT	Ala GCC 921	Lys AAG	Thr ACA	Lys AAG 930	Pro CCG	Arg CGG	Glu GAG 939
Glu Gln GAG CAG	Phe 1 TTC 1 948	Asn S AAC <i>I</i>	Ser AGC	Thr ACG 957	Tyr TAC	Arg CGT	Val GTG 966	Val GTC	Ser AGC	Val GTC 975	Leu CTC	Thr ACC	Val GTC 984	Leu CTG	His CAC	Gln CAG 993	GYC Yeb	TGG	Leu CTG 1002
Asn Gly AAC GGC 1	Lys ( AAG ( 1011	Glu ? GAG ?	TAC	Lys AAG 1020	Cys TGC	AAG	Val GTC 1029	Ser TCC	AAC	Lys AAA 1038	Gly GGC	CTC	Pro CCG L047	Ser TCC	TCC	Ile ATC 1056	Glu GAG	AAA	Thr ACC 1065
Ile Ser ATC TCC			AAA			CCC			CCA			TAC			CCC			CAG	
Glu Met GAG ATG	Thr I ACC I	Lys 1 AAG 1	AAC	Gln CAG 146	Val GIC	AGC	Leu CTG L155	Thr ACC	TGC	Leu CTG 1164	Val GTC	AAA	Gly GGC L173	Phe TTC	TAC	Pro CCC L182	Ser AGC	GAC	Ile ATC 1191
Ala Val GCC GTG	Glu : GAG : L200	Trp (	GAG	Ser AGC 1209	Asn AAT	GGG	Gln CAG 1218	Pro	GAG	Asn AAC 1227	Asn AAC	TAC	Lys AAG L236	Thr ACC	ACG	Pro CCT L245	Pro CCC	GTG	Leu CTG L254
Asp Ser GAC TCC	Asp ( GAC ( 1263	Gly : GGC :	TCC	Phe TIC 1272	Phe TTC	CTC	Tyr TAC 1281	Ser AGC	AGG	Leu CTA 1290	Thr ACC	GTG	Asp GAC L299	Lys AAG	AGC	Arg AGG L308	Trp TGG	CAG	Glu GAG L317
Gly Asn GGG AAT	Val 1 GTC 1	Phe :	TCA	Cys TGC 1335	Ser TCC	GTG	Met ATG 1344	His CAT	GYC	Ala GCT 1353	Leu CTG	CAC	Asn AAC L362	His CAC	TAC	Thr ACA L371	Gln CAG	AAG	Ser AGC L380

Leu Ser Leu Ser Leu Gly Lys TER CTC TCC CTG TCT CTG GGT AAA TGA 1389 1398



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### Figure 6a

Frame 1	Met ATG	Lys AAA	His CAC 9	Leu CTG	Trp TGG	Phe TTC 18	Phe TTC	Leu	Leu CTC 27	CIG	Val GTG	Ala GCA 36	Ala GCC	Pro	Arg AGA 45	Trp TGG	Val GTC	Leu TTG 54	Ser TCC
Gln Val CAG GTG	Gln CAG 66	Leu CTG	Gln CAG	Glu GAG 75	Ser TCG	Gly	Pro CCA 84	Gly GGA	Leu CTG	Val GTG 93	Lys AAG	Pro CCT	Ser TCG 102	Glu GAG	Thr ACC	Leu CTG 111	Ser TCC	Leu CTC	Thr ACC 120
Cys Ser TGC AGT	Val GTC 129	Ser TCT	Gly GGT	Gly GGC 138	Ser TCC	Ile	Ser AGC 147	Gly GGT	Asp GAC	Tyr TAT 156	Tyr TAT	Trp TGG	Phe TTC 165	Trp TGG	Ile ATC	Arg CGC 174	Gln CAG	Ser TCC	Pro CCA 183
Gly Lys GGG AAG	Gly GGA 192	Leu CTG	Glu GAG	Trp TGG 201	Ile ATC	Gly GGC	Tyr TAC 210	Ile ATC	Tyr TAT	Gly GGC 219	Ser AGT	Gly GGT	Gly GGG 228	Gly GGC	Thr ACC	Asn AAT 237	Ty: TAC	Asn AAT	Pro CCC 246
Ser Leu TCC CTC	Asn AAC 255	Asn AAT	Arg CGA	Val GTC 264	Ser TCC	Ile ATT	Ser TCA 273	Ile ATA	Asp GAC	Thr ACG 282	Ser TCC	Lys AAG	Asn AAC 291	Leu CTC	Phe TTC	Ser TCC 300	Leu CTG	Lys AAA	Leu CTG 309
Arg Ser AGG TCT	Val GTG 318	Thr ACC	Ala GCC	Ala GCG 327	Asp GAC	Thr ACG	Ala GCC 336	Val GTC	Tyr TAT	Tyr TAC 345	Cys TGT	Ala GCG	Ser AGT 354	Asn AAT	Ile ATA	Leu TTG 363	yyy Tàs	Tyr TAT	Leu CTT 372
His Trp CAC TGG	Leu TTA 381	Leu TTA	Tyr TAC	Trp TGG 390	Gly GGC	Gln CAG	Gly GGA 399	Val GTC	Leu CTG	Val GTC 408	Thr ACC	Val GTC	Ser TCC 417	Ser TCA	Ala GCT	Ser AGC 426	Thr ACC	Lys AAG	Gly GGG 435
Pro Ser CCA TCC	Val GTC 444	Phe TTC	Pro CCC	Leu CTG 453	Ala GCG	Pro CCC	Cys TGC 462	Ser TCC	Arg AGG	Ser AGC 471	Thr ACC	Ser TCC	Glu GAG 480	Ser AGC	Thr ACA	Ala GCC 489	Ala GCC	Leu CTG	Gly GGC 498
Cys Leu TGC CTG	Val GIC 507	Lys Aag	Asp GAC	Tyr TAC 516	Phe TTC	Pro CCC	Glu GAA 525	Pro CCG	Val GTG	Thr ACG 534	Val GTG	Ser TCG	Trp TGG 543	Asn AAC	Ser TCA	Gly GGC 552	Ala GCC	Leu CIG	Thr ACC 561
Ser Gly AGC GGC	Val GTG 570	His CAC	Thr ACC	Phe TTC 579	Pro CCG	Ala GCT	Val GTC 583	Leu CTA	Gln CAG	Ser TCC 597	Ser TCA	Gly GGA	Leu CTC 606	Tyr TAC	Ser TCC	Leu CTC 615	Ser AGC	Ser AGC	Val GTG 624
Val Thr GTG ACC	Val GTG 6:3	CCC.	Ser TCC	Ser AGC 642	Ser AGC	Leu TTG	Gly GGC 651	Thr ACG	Lys AAG	Thr ACC 660	Tyr TAC	Thr ACC	Cys TGC 669	Asn AAC	Val GTA	Asp GAT 678	His CAC	Lys AAG	Pro CCC 687
Ser Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro



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### Figure 6 b

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AGC	AAC	ACC 696	aag	GTG	GAC 705	AAG	AGA	GTT 714	GAG	TCC	ааа 723	TAT	GGT	CCC 732	CCA	TGC	CCA 741	CCA	TGC	CCA 750
Ala GCA	CCI	Glu GAG 759	Phe TTC	Glu GAG	Gly GGG 768	Gly GGA	Pro CCA	Ser TCA 777	Val GTC	Phe TTC	Leu CTG 786	Phe TTC	Pro CCC	Pro CCA 795	Lys AAA	Pro CCC	Lys AAG 804	Asp GAC	Thr ACT	Leu CTC 813
Met ATG	Ile ATC	Ser TCC 822	Arg CGG	Thr ACC	Pro CCT 831	Glu GAG	Val GTC	Thr ACG 840	Cys TGC	Val GTG	Val GIG 849	Val GIG	Asp GAC	Val GTG 858	Ser AGC	Gln CAG	Glu GAA 867	Asp GAC	Pro CCC	Glu GAG 876
Val GTC	Gln CAG	Phe TTC 885	Asn AAC	Trp TGG	Tyr TAC 894	Val GTG	Asp GAT	Gly GGC 903	Val GTG	Glu GAG	Val GTG 912	His CAT	Asn AAT	Ala GCC 921	Lys AAG	Thr ACA	Lys AAG 930	Pro CCG	Arg CGG	Glu GAG 939
Glu GAG	Gln CAG	Phe TTC 948	Asn AAC	Ser AGC	Thr ACG 957	Tyr TAC	Arg CGT	Val GTG 966	Val GTC	Ser AGC	Val GIC 975	Leu CTC	Thr ACC	Val GTC 984	Leu CTG	His CAC	Gln CAG 993	GAC Asp	TGG	Leu CTG 1002
Asn AAC	GGC	Lys AAG L011	Glu GAG	TAC	Lys AAG 1020	Cys TGC	AAG	Val GTC L029	Ser TCC	AAC	Lys AAA 8001	Gly GGC	CIC	Pro CCG L047	Ser TCC	TCC	Ile ATC 1056	Glu GAG	AĀA.	Thr ACC 1065
Ile ATC	TCC	Lys AAA L074	Ala GCC	AAA	Gly GGG L083	Gln CAG	CCC	Arg CGA L092	Glu GAG	CCA	Gln CAG 1101	Val GTG	TAC	Thr ACC 1110	Leu CTG	CCC	Pro CCA 1119	Ser TCC	CAG	Glu GAG L128
Glu GAG	ATG	Thr ACC L137	Lys AAG	AAC	Gln CAG 1146	Val GTC	AGC	Leu CTG L155	Thr ACC	TGC	Leu CTG 1164	Val GTC	AAA	Gly GGC 1173	Phe TTC	TAC	Pro CCC L182	Ser AGC	GAC	Ile ATC 1191
Ala GCC	GIG	Glu GAG L200	Trp TGG	GAG	Ser AGC 1209	Asn AAT	GGG	Gln CAG 1218	Pro CCG	GAG	Asn AAC 1227	Asn AAC	TAC	Lys AAG 1236	Thr ACC	ACG	Pro CCT 1245	Pro CCC	GTG	Leu CTG L254
Asp GAC	TCC	Asp GAC 1263	GGC	TCC	Phe TTC 1272	Phe TTC	CIC	Tyr TAC L281	Ser AGC	AGG	Leu CTA 1290	Thr ACC	GTG	Asp GAC 1299	Lys AAG	AGC	Arg AGG 1308	Trp TGG	CAG	Glu GAG 1317
Gly GGG	AAT	Val GTC 1326	Phe TTC	TCA	Cys TGC 1335	Ser TCC	GTG	Met ATG 1344	His CAT	GAG	<u>Al</u> a GCT 1353	Leu CTG	CAC	Asn AAC 1362	His CAC	TAC	Thr ACA 1371	Gln CAG	AAG	Ser AGC 1380
_			_	_		_														

Leu Ser Leu Ser Leu Gly Lys TER CTC TCC CTG TCT CTG GGT AAA TGA 1389 1398



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### Figure 7a

## Primers for the Amplifcation of Monkey Immunoglobulin Heavy Chain Variable Regions

#### 5' 'Sense' Primers

#### A. Human or Monkey heavy chain early leader sequence primers with Sall site

V <sub>11</sub> 1	5' ACTAAGTCGACAT GGACTGGACCTGG 3
<b>*</b> U '	3 ACIANGICCACAI GCACIGCACCIGG 3

VH2 5' ACTAAGTCGACATGGACATACTTTGTTCCAC 3'

V<sub>H</sub>3 5' ACTAAGTCGACATGGAGTTTGGGCTGAGC 3'

V<sub>H</sub>4 5' ACTAAGTCGACAT GAAACACCTGTGGTTCTT 3'

V<sub>H</sub>5 5' ACTAAGTCGACAT GGGGTCAACCGCCATCCT 3'

V<sub>H</sub>6 5' ACTAAGTCGACATGTCTGTCTCCTCAT 3'

#### B. Human or Monkey heavy chain late leader sequence primers with Mlu I site

- V<sub>H</sub>1 5' G GCA GCA GC(CT) ACG CGT GCC CAC TCC GAG GT 3'
- VH2 5' G ACC GTC CCG ACG CGT GT(TC) TTG TCC CAG GT 3'
- V<sub>H</sub>3 5' GCT ATT TTC ACG CGT GTC CAG TGT GAG 3'
- V<sub>H</sub>4 5' GCG GCT CCC ACG CGT GTC CTG TCC CAG 3'
- V<sub>H</sub>5 5' G GCT GTT CTC ACG CGT GTC TGT GCC GAG GT 3'



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### Figure 7b

#### C. Human or Monkey framework 1 sequence primers with Xho I site

V<sub>H</sub>1,3a,5 CAGGTGCAGCTG<u>CTCGAG</u>TCTGG

V<sub>H</sub>2 CAGGTCAACTTA<u>CTCGAG</u>TCTGG

V<sub>H</sub>3b F1 GAGGTGCAGCTG<u>CTCGAG</u>TCTGG

V<sub>H</sub>4 CAGGTGCAGCTG<u>CTCGAG</u>TCTGG

V<sub>H</sub>6 CAGGTACAGCTG<u>CTCGAG</u>TCAGG

#### 3' 'Anti-Sense' Primers.

A. <u>Human or Monkey Heavy Chain Constant Region Primers Anti-Sense Strand</u> with Nhe 1 site

+118 +110

IgG<sub>1-4</sub> 5' GGC GGA TGC GCT AGC TGA GGA GAC GG 3'

Nhe 1



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### Figure 7c

## Primers for the Amplifcation of Monkey Immunoglobulin Light Chain Variable Regions

#### 5' 'Sense' Primers

- A. Human or Monkey kappa light chain early leader primers with Bal II site
- 1. 5'ATCACAGATCTCTCACCATGGTGTTGCAGACCCAGGTC 3'
- 2. 5'ATCACAGATCTCTCACCATGG(GA)G(AT)CCCC(TA)GC(TG)CAGCT 3'
- 3. 5'ATCACAGATCTCTCACCATGGACATGAGGGTCCCCGCTCAG 3'
- 4. 5'ATCACAGATCTCTCACCATGGACAC(GAC)AGGGCCCCCACTCAG 3'
- B. Human or Monkey lambda light chain early leader primers with Bal II site
- 1. 5'ATCACAGATCTCTCACCATGGCCTGGGCTCTGCTGCTCC 3'
- 2. 5'ATCACAGATCTCTCACCATGGCCTGGGCTCCACTACTTC 3'
- 3. 5'ATCACAGATCTCTCACCATGACCTGCTCCCCTCTCCCC3'
- 4. 5'ATCACAGATCTCTCACCATGGCCTGGACTCCTCTTTC 3'
- 5. 5'ATCACAGATCTCTCACCATGACTTGGACCCCACTCCTC 3'



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### Figure 7d

#### 3' 'Anti-Sense' Primers

A. Human or Monkey kappa light chain constant region primer anti-sense strand with Kon 1 and BsiW1 sites

C<sub>kappa</sub>

+108 5' CCG TTT GAT TTC CAG CTT GGT ACC TCC ACC GAA CGT 3'

Kpn 1

+112 5' TGC AGC ATC CGT ACG TTT GAT TTC CAG CTT 3' BsiW1

B. Human or Monkey lambda light chain constant region primer anti-sense strand with Kon 1, Hind III and Avr II sites

C<sub>Lambda</sub>

5' ACC TAG GAC GGT AAG CTT GGT ACC TCC GCC 3' Hind III Kpn 1

+97 5' ACC TAG GAC GGT CA(C/G) (C/G)TT GGT ACC TCC GCC GAA CAC 3' Kpn 1

+110 +102 5' CTT GGG CTG ACC TAG GAC GGT CAG CCG 3' Avr II



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ATGGGGTCAACCGCCATCCT 3'

### Figure 8

#### A Heavy Chain Variable Region:

5'

VH5

- VH1 5' CCATGGACTGGACCTGG 3' VH2 5' ATGGACATACTTTGTTCCAC 3' VH3 CCATGGAGTTTGGGCTGAGC 3' 5" VH4 ATGAAACACCTGTGGTTCTT 3' 5'
- VH6 5' ATGTCTGTCTCCTCAT 3'

### B. Heavy Chain Constant Region Anti-Sense Strand:

+119 **IgM** 5' T TGG GGC GGA TGC ACT 3'

+119 IgG<sub>1-4</sub> GATGG GCC CTT GGT GGA 3' 5'

### C. Light Chain Variable Region:

G ATG ACC CAG TCT CCA (G/T)CC TC 3' Kappa 5'

CTC A(C/T)T (T/C)(G/A)C TGC (A/C)CA GGG TCC 3' Lambda 5'

### D. Light Chain Constant Region Anti-Sense Strands:

+110 Kappa 5' AA GAC AGA TGG TGC AGC CA 3' +118

G GAA CAG AGT GAC CGA GGG G 3' Lambda 5'

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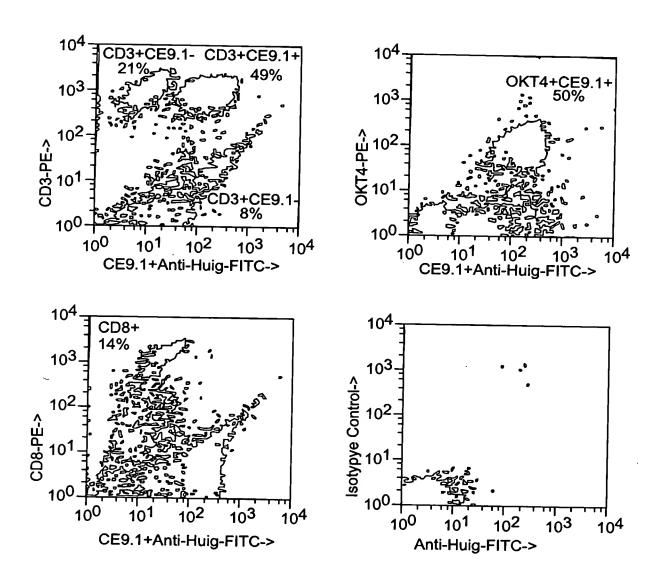


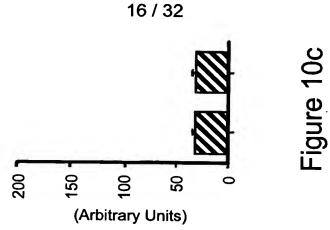
Figure 9

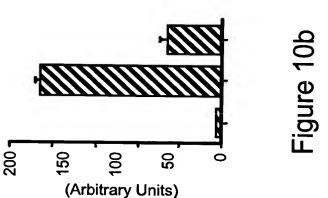


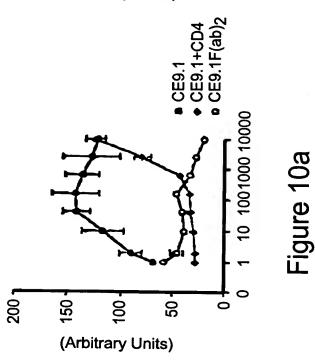
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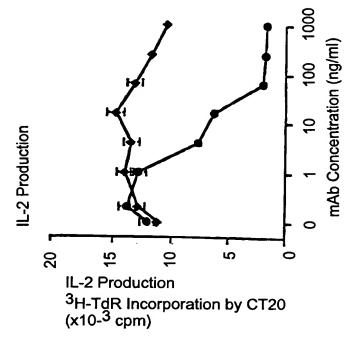


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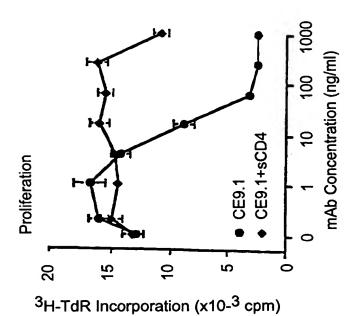


Figure 11



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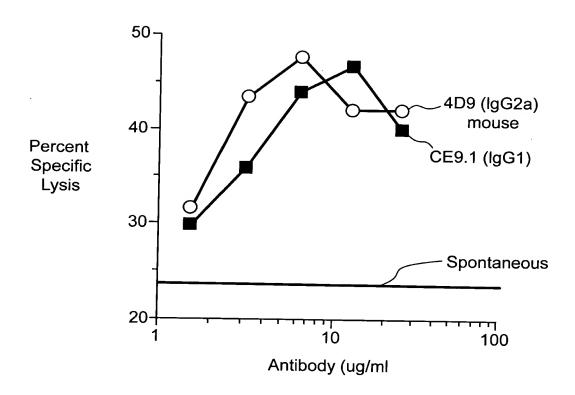


Figure 12



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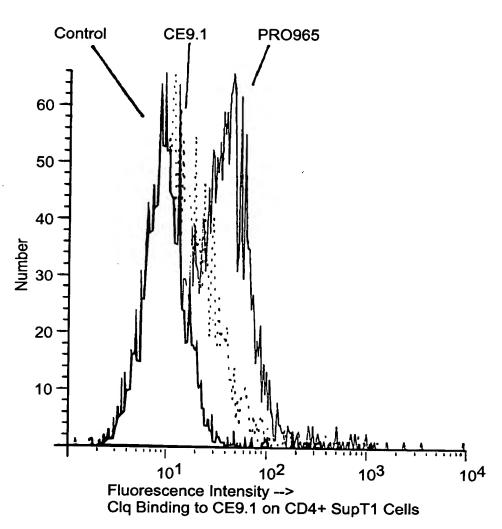


Figure 13



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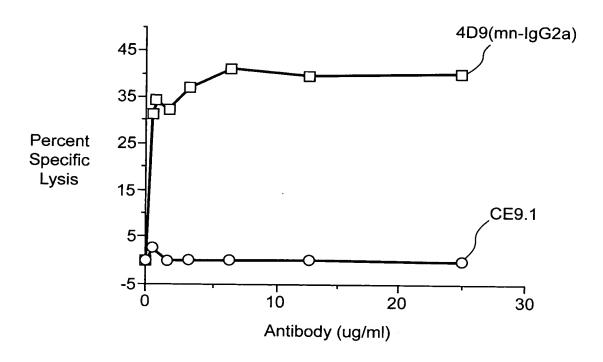


Figure 14



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CD4 and CD8 Cell Counts in Chimpanzees Repeatedly Treated with 10 mpk of CE9.1

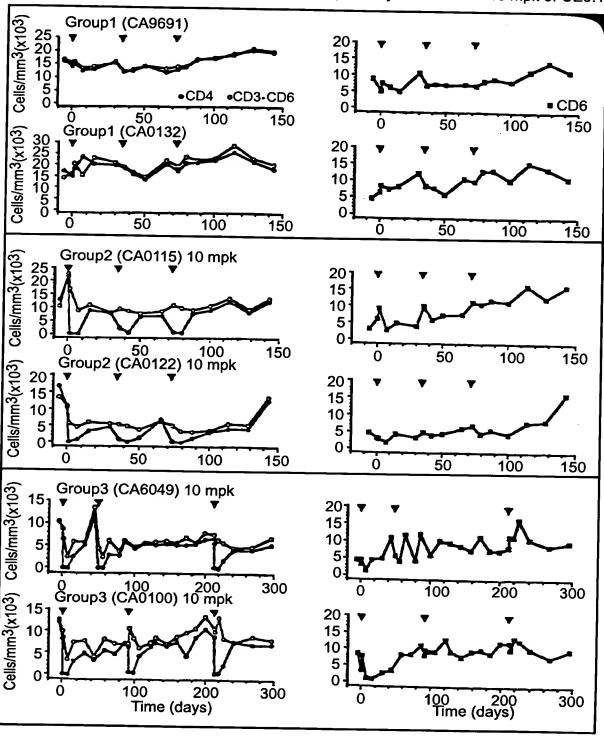


Figure 15



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PCR Primers for Human 14 Constant Region

Figure 16

1) IDEC 462 3' PCR Primer

5 GGGG GGA ICC TCA TIT ACC CAG AGA CAG GG 3'
Bamh I

2) IDEC 479 5' PCR Primer

5' GGGG GCT AGC ACC AAG GGC CCA TCC GTC TTC 3'

PCR Mutagenesis of Human 14

3) IDEC 698 3' PCR Primer

S CCG GGA GA<u>t Cat ga</u>g agt gtc ctt ggg ttt tgg ggg gaa cag gaa gac Biph i

G

TGA TGG TCC CCC CTC GAA CTC AGG TGC TGG GCA TGG TGG GCA TGG GGG 3° E

4) Midland GE212 5' PCR Primer

S' TCC TCA GCT AGC ACC AAG GGG CCA TCC 3'
Destroys Apa I site



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### Figure 17a

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAG GGG 



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## Figure 17b

Pro	Ser TCC	Val GTC 444	TTC	Pro	Leu CTG 453	GCG	Pro CCC	Cys TGC 462	Ser TCC	Arg AGG	Ser AGC 471	ACC	Ser TCC	Glu GAG 480	Ser AGC	Thr ACA	Ala GCC 489	Ala GCC	Leu CTG	Gly GGC 498
Cys TGC	Leu CTG	Val GTC 507	AAG	Asp GAC	Tyr TAC 516	Phe TTC	Pro	Glu GAA 525	Pro CCG	Val GTG	Thr ACG 534	GTG	Ser TCG	Trp TGG 543	Asn AAC	Ser TCA	Gly GGC 552	Ala GCC	Leu CTG	Thr ACC 562
Ser	Gly GGC	Val GTG 570	CAC	Thr	Phe TTC 579	Pro CCG	Ala GCT	Val GTC 588	Leu CTA	Gln CAG	Ser TCC 597	Ser TCA	Gly GGA	Leu CTC 606	Tyr TAC	Ser TCC	Leu CTC 615	Ser AGC	Ser AGC	Val GTG 624
Val GTG	Thr	Val GTG 633	Pro	Ser TCC	Ser AGC 579	Ser AGC	Leu TTG	Gly GGC 588	Thr ACG	Lys AAG	Thr ACC 660	TAC	Thr ACC	Cys TGC 669	Asn AAC	Val GTA	Asp GAT 678	His CAC	Lys AAG	Pro CCC 687
Ser AGC	Asn AAC	Thr ACC 696	Lys AAG	Val GTG	Asp GAC 705	Lys AAG	Arg AGA	Val GTT 714	Glu GAG	Ser TCC	Lys AAA 723	Tyr TAT	Gly GGT	Pro CCC 732	Pro CCA	Cys TGC	Pro CCA 741	Pro CCA	Сув TGC	Pro CCA 750
Ala GCA	Pro CCT	Glu GAG 759	Phe TTC	Gln GAG	Gly GGG 768	Gly GGA	Pro CCA	Ser TCA 777	Val GTC	Phe TTC	Leu CTG 786	Phe TTC	Pro CCC	Pro CCA 795	Lys AAA	Pro CCC	Lys AAG 804	Asp GAC	Thr ACT	Leu CTC 813
Met ATG	Ile ATC	Ser TCC 822	Arg CGG	Thr ACC	Pro CCT 831	Glu GAG	Val GTC	Thr ACG 840	Cys TGC	Val GTG	Val GTG 849	Val GTG	Asp GAC	Val GTG 858	Ser AGC	Gln CAG	Glu GAA 867	Asp GAC	Pro CCC	Glu GAG 876
Val GTC	Gln CAG	Phe TTC 885	Asn AAC	Trp TGG	Tyr TAC 894	Val GTG	Asp GAT	Gly GGC 903	Val GTG	Glu GAG	Val GTG 912	His CAT	Asn AAT	Ala GCC 921	Lys AAG	Thr ACA	Lys AAG 930	Pro CCG	Arg CGG	Glu GAG 939
Glu GAG	Gln CAG	Phe TTC 948	Asn AAC	Ser AGC	Thr ACG 957	Tyr TAC	Arg CGT	Val GTG 966	Val GTC	Ser AGC	Val GTC 975	Leu CTC	Thr ACC	Val GTC 984	Leu CTG	His CAC	Gln CAG 993	Asp GAC	TGG	Leu CTG .002
Asn AAC	Gly GGC 1	Lys AAG 011	Glu GAG	TAC	Lys AAG 1020	Cys TGC	AAG	Val GTC L029	Ser TCC	AAC	Lys AAA 1038	Gly GGC	CTC	Pro CCG .047	Ser TCC	TCC	Ile ATC 056	Glu GAG	AAA	Thr ACC .065
Ile ATC	Ser TCC 1	Lys AAA 074	Ala GCC	AAA	Gly GGG L083	Gln CAG	CCC	Arg CGA .092	Glu GAG	CCA	Gln CAG 101	Val GTG	TAC	Thr ACC 110	Leu CTG	CCC	Pro CCA	Ser TCC	CAG	Glu GAG 128
Glu GAG	Met ATG 1	Thr ACC 137	Lys AAG	AAC	Gln CAG 146	Val GTC	AGC	Leu CTG 155	Thr ACC	TGC	Leu CTG 164	Val GTC	AAA	Gly GGC 173	Phe TTC	TAC	Pro CCC	Ser AGC	GAC	Ile ATC 191
Ala GCC	Val GTG 1	Glu GAG 200	Trp TGG	GAG	Ser AGC 209	Asn AAT	GGG	Gln CAG 218	Pro CCG	GAG	Asn AAC 227	Asn AAC	TAC	Lys AAG 236	Thr ACC	ACG	Pro CCT 245	Pro CCC	GTG	Leu CTG 254
Asp GAC	Ser TCC 1	Asp GAC 263	Gly GGC	TCC	Phe TTC 272	Phe TTC	CTC	Tyr TAC 281	Ser AGC	AGG	Leu CTA 290	Thr ACC	GTG	Asp GAC 299	Lys AAG	AGC	Arg AGG 308	Trp TGG	CAG	Glu GAG 317
Gly GGG	Asn AAT 1	Val GTC 326	Phe TTC	TCA	Cys TGC .335	Ser TCC	GTG	Met ATG 344	His CAT	GAG	Ala GCT 353	Leu CTG	CAC	Asn AAC 362	His CAC	TAC	Thr ACA 371	Gln CAG	AAG	Ser AGC 380
Leu CTC	Ser TCC 1	Leu CTG 389	Ser TCT	CTG	Gly GGT 398	Lys AAA	TER TGA													



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INVENTOR: NABB HANNA et al.
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55.4 kD →		
36.5 kD →		
31 kD →		
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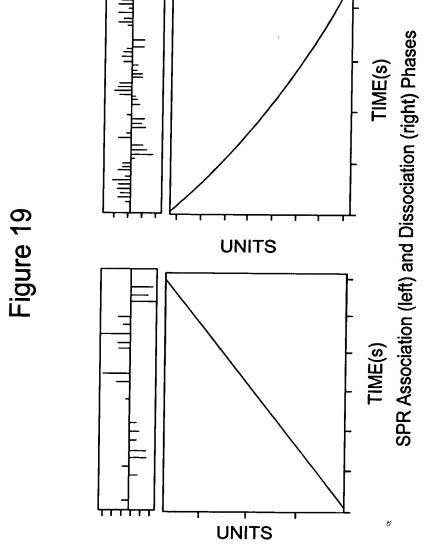
Figure 18



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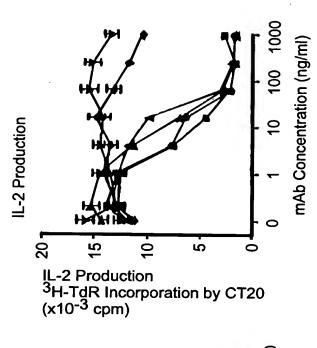


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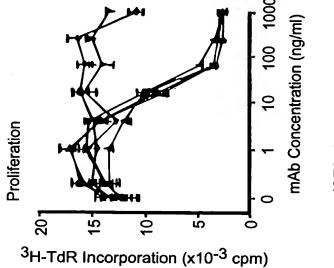




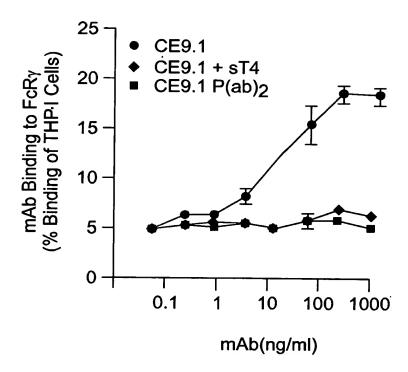
Figure 20



Appin. No.: 03/612,914
INVENTOR: Nabil HANNA et al.
FILED: July 10, 2000
ATTORNEY DOCKET: 03/7003/02/67/6543
IDEC REF. NO.: 1999-30-0019CP4C1
ITTLE: RECOMBINANT ANTI-CD4 ANTIBODIES OR HUMAN THERAPY
PILLSBURY WINTHROP LLP
MCLEAN, VIRGINIA



Figure 21





Appin. No.: 09/612,914
INVENTOR: NabB HANNA et al.
FILED: July 10, 2000
ATTORNEY DOCKET:: 037003/0276543
IDEC REF. NO.: 1995-30-0019CP4C1
TITLE: RECOMBINANT ANTI-CD4 ANTIBODIES OR HUMAN THERAPY

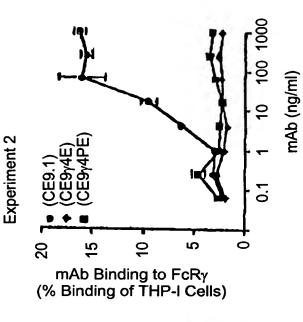
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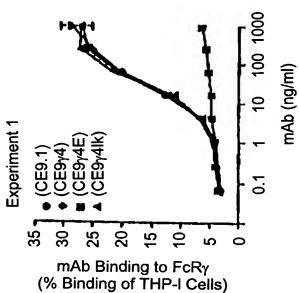
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Figure 22



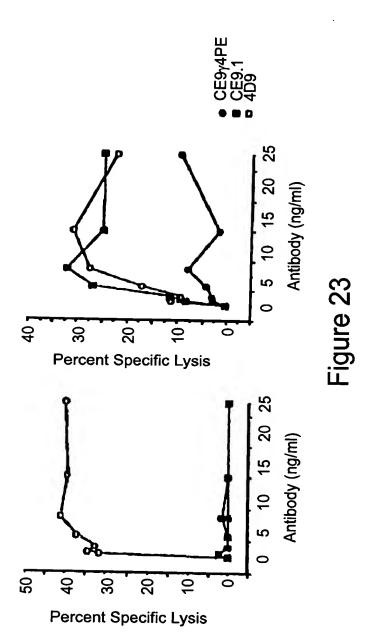




Appin. No.: 09/612,914
INVENTOR: Nabil HANNA et al.
FILED: July 10, 2000
ATTORNEY DOCKET: 037003/0276543
IDEC REF. NO.: 1999-30-0019CP4C1
ITTLE: RECOMBINANT ANTI-CD4 ANTIBODIES OR HUMAN THERAPY

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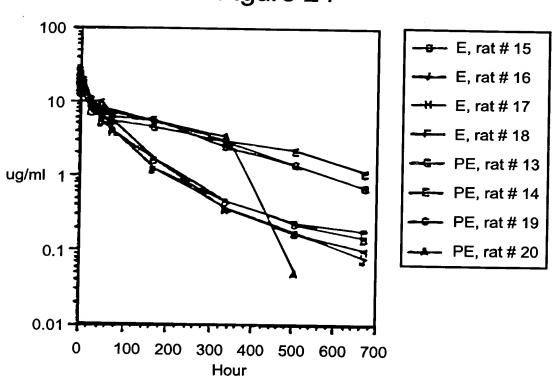




Appin. No.: 03/612,914
INVENTOR: Nabi HANNA et al.
FILED: July 10, 2000
ATTORNEY DOCKET.: 037003/0275643
IDEC REF. NO.: 1939-30-0019CP4C1
TITLE: RECOMBINANT ANTI-CC4 ANTIBODIES OR HUMAN THERAPY
PILLSBURY WINTHROP LLP
MCLEAN, VIRGINIA









Appin. No.: 03/612,914
INVENTOR: Nabil HANNA et al.
FILED: July 10, 2000
ATTORNEY DOCKET: 037003/0276543
IDEC REF. NO.: 1999-30-0019CP4C1
TITLE: RECOMBINANT ANTI-CD4 ANTIBODIES OR HUMAN THERAPY

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